Claims

1. A method for modulating the activity of at least one neurotrophin and/or a pro-neurotrophin in a cell or an organism, such as an animal, comprising administering to said animal a sufficient amount of an agent capable of
   (j) binding to a receptor of the Vps10p-domain receptor family
   and/or
   (ii) interfering with binding between a receptor of the Vps10p-domain receptor family and a neurotrophin and/or proneurotrophin
   and/or
   (iii)modulating the expression of a receptor of the Vps10p-domain receptor family.

2. The method according to claim 1, wherein the modulation is a decrease of the activity.

3. The method according to claim 1, wherein the modulation is an increase of the activity.

4. The method according to any of the preceding claims, wherein the neurotrophin is selected from neural growth factor (NGF), brain derived neurotrophic factor (BDNF), neurotrophin-3 (NT-3), neurotrophin-4/5 (NT-4/5).

5. The method according to claim 4, wherein the neurotrophin is NGF or BDNF.

6. The method according to any of the claims 1-3, wherein the pro-neurotrophin is selected from pro-NGF, pro-BDNF, pro-NT-3 or pro-NT-4/5.

7. The method according to claim 6, wherein the pro-neurotrophin is pro-NGF or pro-BDNF.

8. The method according to any of the preceding claims, wherein the animal is a mammal.

9. The method according to claim 8, wherein the mammal is a human being.

10. The method according to any of the preceding claims, wherein the receptor is selected from SorLA, Sortilin, SorCS1, SorCS-2, or SorCS-3.

11. The method according to claim 10, wherein the receptor is Sortilin.

12. The method according to any of the preceding claims, wherein the agent is selected from proteins, peptides, polypeptides, antibodies, antisense RNA, anti-sense-DNA or organic molecules, SiRNA.

13. The method according to any of the preceding claims, wherein the agent is capable of inhibiting binding of said neurotrophin or said pro-neurotrophin to the receptor.

14. The method according to any of the preceding claims, wherein the agent is capable of binding to an extracellular part of the receptor.

15. The method according to any of the preceding claims, wherein the agent is an antibody directed against an extracellular part of the receptor an intracellular part of the receptor or a transmembrane part of the receptor.

16. The method according to claim 15, wherein the agent is an antibody directed against a peptide comprising a sequence having SEQ ID NO: 1 amino acid residues 612-740.

17. The method according to any of the claims 1-14, wherein the agent is a peptide comprising a sequence having SEQ ID NO: 1 amino acids 24-77 or a variant thereof, said peptide being capable of binding to the receptor.

18. The method according to claim 17, wherein the variant is selected from one or more of the following sequences: SEQ ID NO: 2 amino acid residues 29-81 (propart from SorLa).

19. The method according to claim 17, wherein the peptide comprises one or more of the following sequences SEQ ID NO: 6 amino acid residues 19-121 (propart for NGF), SEQ ID NO 7 amino acid residues 19-127 (propart for BDNF), SEQ ID NO: 8 amino acid residues 17-124 (propart for neurotrophin-3 (NT-3), SEQ ID NO: 9 amino acid residues 25-80 (propart for neurotrophin-4 (NT-4) or a fragment or a variant thereof, said peptide being capable of binding to the receptor.

20. The method according to claim 1 or 19, wherein the agent is a peptide comprising a Sortilin receptor-binding sequence of proNGF.

21. The method according to claim 19, wherein the agent is a peptide comprising the sequence SEQ ID NO: 6 amino acid residues 19-121 (the sequence from the pro-part of NGF) or a variant thereof, said peptide being capable of binding to the receptor.

22. The method according to claim 20, wherein the agent is a peptide consisting of the following sequence SEQ ID NO: 6 amino acid residues 19-121 (propeptide of proNGF).

23. The method according to any of the claims 1-14, wherein the agent is a peptide having the sequence of SEQ ID NO: 10 or SEQ ID NO: 11, or a fragment or a variant thereof, said peptide being capable of binding the receptor.

24. The method according to any of the claims 1-14 wherein the agent is a peptide comprising an NGF variant or a Sortilin-receptor binding fragment of said NGF variant.

25. The method according to claim 23, wherein the peptide is capable of binding Sortilin and stimulating the activity of the Sortilin receptor.

26. A method for treating a disease or disorder in an individual, comprising administering to said individual a sufficient amount of an agent as defined in any of the claims 1-25.

27. The method according to claim 26, wherein the disease or disorder is selected from one or more of the following diseases or disorders: inflammatory pain, diseases or disorders of pancreas, kidney disorders, lung disorders, cardiovascular disorders, various types of tumours, psychiatric disorders or neuronal disorders.

28. The method according to claim 26, wherein the disease or disorder is selected from Alzheimer's disease, Parkinson's disease, Huntington's chorea, stroke, ALS, peripheral neuropathies, necrosis or loss of neurons, nerve damage to trauma, kidney dysfunction, injury, and the toxic effects of chemotherapeutics used to treat cancer and AIDS, aberrant sprouting in epilepsy, schizophrenia, pancreas or lung injury and/or dysfunction, injury and/or dysfunction of the central and/or peripheral nervous systems.

29. The method according to claim 27, wherein the disease or disorder is selected from peripheral neuropathy, distal sensorimotor neuropathy, or autonomic neuropathies, such as reduced motility of the gastrointestinal tract or atony of the urinary bladder, post-polio syndrome or AIDS-associated neuropathy; hereditary neuropathies, such as Charcot-Marie-Tooth disease, Refsum's disease, Abetalipoproteinemia, Tangier disease, Krabbe's disease, Metachromatic leukodystrophy, Fabry's disease, and Dejerine-Sottas syndrome, depression, mania or Down's syndrome.

30. The method according to any of claims 26-28, wherein the agent is administered in an amount of from 1 μg/kg to about 100 mg/kg per day.

31. An in vitro method for screening for a compound which alters the binding of at least one neurotrophin and/or a pro-neurotrophin to a receptor of the Vps10p-domain receptor family,

a) providing an assay for measuring the binding of a neurotrophin and/or a pro-neurotrophin to a receptor of the Vps10p-domain receptor family

b) adding the compound to be tested to the assay, and

a) determining the amount of a neurotrophin and/or a pro-neurotrophin bound to the receptor of the Vps10p-domain receptor family, and

b) comparing the amount determined in step c) with an amount measured in the absence of the compound to be tested,

c) wherein a difference in the two amounts identifies a compound which alters the binding of neurotrophins and/or pro-neurotrophins to the receptor of the Vps10p-domain receptor family.

32. The method according to claim 30, wherein the neurotrophin is selected from neural growth factor (NGF), brain derived neurotrophic factor (BDNF), neurotrophin-3 (NT-3), neurotrophin-4 (NT-4).

33. The method according to claim 32, wherein the neurotrophin is NGF or BDNF.

34. The method according to claim 30, wherein the pro-neurotrophin is selected from pro-NGF, or pro-BDNF.

35. The method according to claim 34, wherein the pro-neurotrophin is pro-NGF or pro-BDNF.

36. The method according to any one of claims 30-35, wherein the receptor is selected from SorLa, Sortilin, SorCS1, SorCS3, or SorCS2.

37. The method according to claim 36, wherein the receptor is Sortilin.

38. The method according to any one of claims 30-37, wherein the neurotrophin and/or pro-neurotrophin is capable of binding to an extracellular part of the receptor, an intracellular part of the receptor or a transmembrane part of the receptor.

39. The method according to any one of claims 30-38, wherein the receptor is expressed in a cell and/or presented on a cell plasma membrane.

40. The method according to claim 39, wherein the cell is selected from peripheral neurons, central neurons, primary cultures of neuronal cells, neuron-derived cell-lines and transfected cells capable of expressing and/or presenting a receptor of the Vps10p-domain receptor family.

41. A method for determining the effect of an agent on activity of neurotrophins and/or pro-neurotrophins in cells expressing a receptor of the Vps10p-domain receptor family, said method comprising the steps of

a) administering said agent to a mammal naturally expressing the receptor,

b) measuring the activity of neurotrophins and/or pro-neurotrophins in said mammal,

c) comparing the measurement of step b) with a measurement obtained in the absence of the compound to be tested,

d) wherein the difference in the two measurements identifies the effect of said agent on the activity of neurotrophins on cells presenting receptors of the Vps10p-domain receptor family.

42. The method according to claim 41, wherein said method further comprises administering said agent to a mammal lacking expression of said receptor.

43. The method according to claim 42, wherein said mammal only lacks expression of said receptor in one or more selected tissues.

44. An agent capable of modulating the activity of at least one neurotrophin and/or a pro-neurotrophin when said neurotrophin and/or pro-neurotrophin binds to a receptor of the Vps10p-domain receptor family.

45. A method for modulating the transport of at least one neurotrophin and/or pro-neurotrophin out of, into or within a cell line or a cell expressing a receptor of the Vps10p-domain receptor family in an animal,

comprising administering to said animal a sufficient amount of an agent capable of binding a receptor of the Vps10p-domain receptor family.

46. The method according to claim 45, where the modulation comprises an increase in the anterograde transport of the neurotrophin and/or pro-neurotrophin in the neuron.

47. The method according to claim 45, where the modulation comprises a decrease in anterograde transport of the neurotrophin and/or pro-neurotrophin in the neuron.

48. The method according to claim 45, where the modulation comprises an increase in the retrograde transport of the neurotrophin and/or pro-neurotrophin in the neuron.

49. The method according to claim 45, where the modulation comprises a decrease in retrograde transport of the neurotrophin and/or pro-neurotrophin in the neuron.

50. The method according to any one of claims 45-49, wherein the agent is as defined in any of the claims 1-27.

51. A method of isolating a compound capable of altering the binding of at least one neurotrophin and/or proneurotrophin to a receptor of the Vps10p-domain receptor family comprising the steps of

a) screening a compound as defined in any of claims 32-41,
b) selecting a compound altering the binding of at least one neurotrophin and/or pro-neurotrophin to a receptor of the Vps10p-domain receptor family,
c) isolating the compound of step b).

52. The method of claim 51 further comprising the step of refining the isolated compound/reducing the toxicity of the isolated compound.

53. A method of producing a pharmaceutical composition comprising the steps of claims 51 or 52 and further the step of formulating the refined compound/-compound with reduced toxicity with a pharmaceutically acceptable carrier or diluent.

54. A soluble receptor of the Vps10p-domain receptor family or a fragment or a variant thereof.

55. Use of a soluble receptor as defined in claim 54 for the preparation of a medicament.

56. Use of a soluble receptor as defined in claim 54 for the preparation of a diagnostic agent for the diagnosis of neurotrophin and/or pro-neurotrophin related diseases.

57. A pharmaceutical composition comprising a soluble receptor of the Vps10p-domain receptor family or a fragment or a variant thereof.